where A is the biological response (percent decreased mean arterial pressure), $Amax$ is the maximal response, x is the concentration of histamine (μg/kg), and K_x is the dissociation constant. In this instance, K_x is also the concentration of histamine needed to produce one-half the maximum response. The intercept in equation (1) is $1/Amax$, which provides the value of maximal response from which one-half the maximum response is calculated. The concentration K_x at which the one-half maximum response occurs can also be obtained from the least squares solution to equation (1) by simple algebraic manipulation. K_x is the dose ratio of the concentrations of agonist needed in the presence and absence of antagonist to produce the same response. Theoretically, for competitive antagonism, the doseresponse curves with and without antagonists should be parallel and of equal heigh or maximal response[9,10]. The response in vivo, however, is complicated by the interaction of different physiological systems, resulting in this instance in increased maximal response after antagonism.

The maximal responses to histamine after antogonism do not differ significantly from each other but do differ significantly from the maximal response when histamine is given alone (Table). This would seem to indicate that some factor is present which modulates the effect of the agonist and is absent after the antagonists are given.

One explanation for this may be based on the stimulating effect of histamine on the adrenal medulla causing the liberation of catecholamines with their characteristic pressor effects[12,13]. The response to histamine would thus be a summation of pressor and depressor effects. The release of catecholamines by histamine is abolished by antihistamines; this could result in the increased maximal response after antihistamines are given. To test this possibility, 3 monkeys were given an α-adrenergic blocking agent (phenozybenzamine, 2 mg/kg) which would presumably block any modulating effect of catecholamines on the maximal response. After this treatment, the maximal effect was increased to 47%, providing a possible explanation for the discrepancy (Figure 1).

Although the Lineweaver-Burke method is an excellent means of determining the maximal response of an agonist, the value of the dissociation constant, when based on blood pressure presponses, is of lesser accuracy. The concentration of the drug in contact with receptors may be different from the concentration in the circulating blood which is a reflection of the concentration of the injectant. The changes in blood pressure reflect a composite of changes in the entire cardiovascular system[9]. The dissociation constant between a drug and its receptors may be different in different tissue, hence the dissociation constant determined from in vivo data must be viewed with these factors in mind.

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Regional Variations of Choline-Acetyltransferase in the Chick Embryo Optic Lobe

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Summary. The specific activity of CAT and AChE was determined in different regions of the chick embryo optic lobe at several stages of development. Regional differences in CAT activity appeared in 9-day-old tectum, being the postero-basal area the one with higher enzymatic activity. On the other hand, at 6th and 13th day of development, the levels of AChE and CAT are similar throughout the optic lobe.

The avian optic tectum is an excellent model to study the pattern of development of a nervous center and the effect of peripheral innervation upon its differentiation. A sizable body of literature, gathered in the last few years[2-4], has provided insight into the major features of its development. Thus, it is known that several phases of cell proliferation and migration are involved in the organization of its precise laminated structure so that, by the 12th day of development, all the main strata of the mature tectum are recognizable. At every stage its antero-latero-ventral portion is further developed than the caudo-dorso-medial region.

The optic nerve, which is the main afferent connection of the tectum, reaches its antero-ventral base around the 6th day of development and progressively invades the tectal surface in an antero-ventral (AV) to postero-dorsal (PD) sequence, paralleling the gradient of morphological differentiation and cell proliferation. Between days 12 and 13 of development the growing front of the optic fibres has invaded all parts of the tectum including its postero-dorsal surface[5].

The present study analyzes whether the AV-PD wave of cytoarchitectonic differentiation and of sequential ingrowth of retinal fibres across the tectal surface is also paralleled by a differential enzymatic activity of the neural cells. For this purpose, the activity of the enzymes of the cholinergic system, choline acetyltransferase (CAT) and acetylcholinesterase (AChE) was determined in different regions of the optic lobe at several stages of development.

Materials and methods. Eggs from a fertile stock of White Leghorns were incubated at 37 °C. When the embryos reached the desired stage of development, they were removed from the shell and washed several times with Hanks saline solution.

Since the optic lobe undergoes a rotation of 90° between days 7 and 13 of development[5,6], it is extremely important to define the coordinates used to isolate the different regions. In the 6-day-old embryo, the tectum

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Table I. Activities of CAT and AChE in A and P halves of 6-day-old tectum

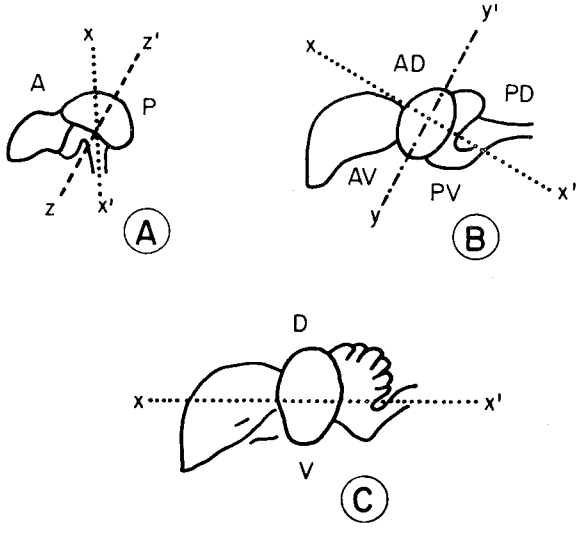
	AChE [a]		CAT [b]	
A	7.41 ± 0.45	$p < 0.02$	0.44 ± 0.04	$p < 0.8$
P	6.37 ± 0.54		0.43 ± 0.02	

Each value represents the average from at least 4 different sets of experiments.
[a] Specific activity is expressed in μmoles of acetylcholine synthesized per h per mg DNA, plus or minus SD.
[b] Specific activity is expressed in μmoles of acetylthiocholine hydrolyzed per min per mg DNA, plus or minus SD. The experimental values were compared with the Student's *t*-test.

Table II. Activities of CAT and AChE in D and V halves of 9-day-old tectum

	AChE		CAT	
V	11.60 ± 1.14	$p < 0.2$	1.52 ± 0.11	$p < 0.001$
D	11.86 ± 1.69		0.48 ± 0.069	

For references see Table I.



A) 6-day-old embryo brain, lateral view. Line z–z′ indicate the plane of dissection. A, anterior; P, posterior.
B) 9-day-old embryo brain, lateral view. Optic lobes were dissected in halves following the plane x–x′ and in quadrants according to planes x–x′ and y–y′. AV, anteroventral; AD, anterodorsal; PV, posteroventral; PD, posterodorsal.
C) 13-day-old embryo brain. The plane of dissection is indicated by the line x–x′. D, dorsal; V, ventral.

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appears roughly oval when viewed laterally, the longer axis of the oval is considered anteroposterior (AP) while the shorter axis is defined as dorsoventral (DV) in coincidence with the encephalic axes. Optic lobes of this age were separated into an anterior (A) and posterior (P) region. Line z–z′ in Figure A indicates the plane of sectioning.

At day 9 of development, the AP and DV axes of the tectum are displaced counterclockwise with respect to the position they had 3 days earlier (compare, for instance, the x–x′ axis in Figure A and B). At this stage, the optic lobe was divided into dorsal (D) and ventral (V) halves following the x–x′ axis. In a 2nd group of experiments, the tectum was separated into quadrants according to the planes x–x′ and y–y′ (the latter is considered to be the former A–P tectal axis; Figure B).

At the 13th day of development, after the 90° tectal rotation, the longer tectal axis is now D–V while the shorter one is defined as the A–P axis. The optic lobes of this age were separated into dorsal (D) and ventral (V) regions (Figure C).

The different regions thus obtained were freed from the surrounding mesenchyme, washed several times with Hanks saline solution, collected in 5 ml tubes and finally homogenized with a teflon pestle homogenizer in a small volume of double distilled water.

CAT and AChE activities were determined according to the techniques of McCaman et al.[7] and Ellman et al.[8] respectively. DNA concentration was measured following the colorimetric procedure of Burton[9]. CAT specific activity is expressed as μmoles of acetylcholine synthesized per h per mg of DNA, while AChE specific activity is expressed as μmoles of acetylthiocoline hydrolyzed per min per mg of DNA.

Results and discussion. At the 6th day of development, the anterior and posterior regions of the optic lobe have almost identical CAT activities, while AChE level is slightly higher in the former (Table I). 3 days later CAT activity in the ventral half of the tectum is significantly higher than that of the dorsal half (Table II). The analysis of the enzyme levels present in the quadrants not only confirmed the existence of this regional difference in CAT activity but also showed that the enzyme levels decreases from the basal to the dorsal areas in the following sequence: PV > AV > AD > PD (Table III). AChE activity is similar in all quadrants.

At the 13th day of development the D and V halves into which the optic lobes were divided showed almost identical CAT and AChE activities (Table IV).

At a first glance, the presence of higher CAT activity at day 9, in the PB quadrant than in the others, plus the fact that the enzyme levels diminishes in a clockwise fashion (PV > AV > AD > PD), could be interpreted as an indication that the pattern of biochemical differentiation does not follow the AV-PD wave of morphological differentiation and of sequential ingrowth of retinal afferents. Only if the rotation of the optic lobe is taken into account does there appear to be a coincidence between these three events. Therefore, before discussing the possible significance of these results, it may be helpful to recapitulate some events of the optic lobe development. At the 6th day of incubation, the longer axis coincides with the AP axis of the body and it is around this age that the retinal fibres reach the AV region. The fibres would then move in an AV-PD direction, forming finally a raphe in the caudomedial zone of the dorsal region of the tectum[5,10]. Due to the counterclockwise rotation of the tectum, the position of the quadrants is displaced 90° with respect to the main body axes, so that the AV region of the 6 day stage – the first to be covered by the afferent

axons – becomes PV, whereas the former PV and now PD would be the last to receive this fibres by day 12–13. On this basis, one of the possible explanations for the wave of increasing levels of CAT activities across the tectal surface could be the presence of this enzyme in the growing axons. The absence of regional differences in enzyme levels, both at the 6th and at the 13th day of development, could be related to the fact that the former still lacks retinal afferents while the latter is fully covered by them. Although it may be worthwhile to further explore this possibility, there is some evidence that seems to indicate that optic fibres are not cholinergic[11].

Table III. Activities of CAT and AChE in quadrants of 9-day-old tectum

	AChE		CAT	
PV	12.71 ± 0.56		1.78 ± 0.12	
		$p < 0.2$		$p < 0.005$
AV	11.20 ± 0.62		1.24 ± 0.15	
		$p < 0.2$		$p < 0.2$
AD	12.39 ± 0.97		0.90 ± 0.094	
		$p < 0.2$		$p < 0.01$
PD	11.48 ± 0.36		0.64 ± 0.092	

For references see Table I.

Table IV. Activities of CAT and AChE in D and V halves of 13-day-old tectum

	AChE		CAT	
V	19.56 ± 0.52		2.61 ± 0.15	
		$p < 0.1$		$p < 0.2$
D	18.12 ± 0.67		2.85 ± 0.18	

For references see Table I.

On the other hand, the augmentation of CAT activity might depend upon transneuronal influences exerted by the incoming retinal fibres upon the tectal cells. This possibility is suggested by the results obtained in our laboratory which showed that, when dissociated retina cells and optic lobe cells are allowed to form mixed aggregates in culture conditions, the activity of CAT but not of AChE is higher than that present when each cell type is cultured alone[12,13]. In order to account for the differences found between the two basal quadrants or the two dorsal ones, it would be necessary to postulate that the interaction is dependent either upon the number of optic fibres that are present or upon the time they have been in contact with the tectal cells.

Alternatively, the gradient in CAT activity present in the tectum of 9-day-old embryos could be the biochemical expression of the autonomous AV-PD wave of morphological differentiation[2,4]. For instance, the level of enzyme activity might depend on the differentiation of a certain type of cholinergic neuron, still absent in the 6-day-old embryo, preferentially localized in the ventral area of the tectum 3 days later and uniformly distributed throughout the optic lobe at the 13th day of development. Since there are some indications that up to the 12th day of development both the morphological and biochemical differentiation of the tectum are independent of the presence of retinal afferents[4,14,15], the sequential increase of CAT activity can also be an intrinsic property of the tectal cells.

Although this study clearly shows the existence of regional differences in CAT activity in the developing tectum, the causal relationship between the retinal fibres and the increased levels of CAT activity in the tectal regions covered by them, remains a critical question. Experiments in progress in our laboratory are aimed to determine the effect of early deafferentation on the temporal sequence of biochemical differentiation of the tectum.

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Dyslexia and Specifically Distorted Drawings of the Face - a New Subgroup with Prosopagnosia-Like Signs

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Summary. Identification of a subgroup (38%) of dyslexics (new syndrome?). These, against controls (5.5%), drew 'neolithic' face configurations analogous to those visually experienced in prosop-agnosia. Essential symptoms of this subgroup are seen as result of specific early ways of processing visual data: lexical shapes (letters, words) and facial features, as if these were concrete entities, not abstract component parts. Thus, with letters, taken as entities, d = q, d = b, N = Z.

This study is based on the following two positions, discussed by CRITCHLEY[2] and based on the definition of dyslexia by the World Federation of Neurology as 'a disorder in children, who, despite conventional classroom experience, fail to attain the language skills of reading, writing and spelling commensurate with their intellectual abilities'[2]: 1. In general, the incidence of dyslexia is known to decrease with increasing age, but in particular cases it may persist. 2. This suggests that specific neurological dysfunctioning exists alone or combined with a developmental lag in a certain subgroup of dyslexics. (Both these factors may show a familial trend as well.) The purpose of the present study is to attempt a delineation of some specific neurological factors in such a sub-